MEMORANDUM

SUBJECT: SUTAN TECHNICAL (BUTYLATE): Updating Executive Summaries for

Reproductive Toxicity Study in Rats
Chronic Toxicity Study in Dogs
Carcinogenicity Study in Mice
Developmental Toxicity Study in Rats
Developmental Toxicity Study in Rabbits
Chronic/Carcinogenicity Study in Rats
Subchronic Neurotoxicity Screening Battery

DP Barcode: D252945 Submission: S556137
PC Code: 041405 Tox Chem No: 434A

TO: Rick J. Whiting
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FROM: Paul Chin
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THRU: Whang Phang, Senior Scientist
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In preparation for the Hazard ID SARC meeting and in writing Toxicology Chapter of the RED for Sutan technical, the DER of many studies were found to be different from the current format. Several studies were reevaluated and the necessary revisions were carried out. New executive summaries and/or supporting tables were prepared for the studies listed below and attached to this memorandum.

<u>Reproductive Toxicity Study in Rats</u>
Minor, J. L. et al (1986). Two Generation Reproduction Studies in Rats. Stauffer Chemical Co.

Study No. T-11940, 6/18/86. MRID 00160548, 00155519. Unpublished.

Chronic Toxicity Study in Dogs

Daly, T. W. (1987). A twelve month oral toxicity study of Sutan technical in dogs. Bio/dynamics Inc., East Millstone, NJ. Study # T-12651. 9/14/87. MRID 40389101. Unpublished.

Carcinogenicity Study in Mice

Goldenthal, E. I. et al (1979). Lifetime Oral Study in Mice. International Research and Development Corp. Study No. 153-008, 8/13/1979. MRID 0035844. Unpublished.

Developmental Toxicity Study in Rats

Downs, J. R. and Greci, L. K. (1983). A Teratology Study in CD Rats with Sutan Technical. Stauffer Chemical Co. Report No. T-11714, 8/22/1983. MRID 00131032. Unpublished.

Developmental Toxicity Study in Rabbits

Wilczynski, S. L. (1987) A Teratology Study in Rabbits with Sutan Technical. Stauffer Chemical Co. Report No. T-112999, 9/16/1987. MRID 40389102. Unpublished.

Chronic/Carcinogenicity Study in Rats

Auletta, C. S. and Hogan, G. K. (1982). A Two-Year Oral Toxicity/Carcinogenicity Study of R-1910 in Rats. Bio/dynamics Inc., East Millstone, NJ. Project # 78-2169. 4/26/82. MRID No. 00125678, 41014901, 41249501. Accession No. 249390-249403. Unpublished.

Subchronic Neurotoxicity Screening Battery

Brammer, A. (1994). Subchronic Neurotoxicity in Rats. Zeneca Central Toxicology Lab (CTL), Cheshire, UK. Report No. CTL/P4423. Study No. PR0970. 9/2/94. MRID 43452201. Unpublished.

CC: BChin (RBB1), 7509C, CM #2, 718L, 305-6376

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Supplement to Document # 005962 and 006875-DERs for MRID No. 00160548 and 00155519: Two Generation Reproduction Study in Rats with Sutan. This supplement provides an Executive Summary to upgrade the original DERs.

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DATA EVALUATION RECORD

STUDY TYPE: 83-4 2-Generation Reproduction Study in Rats

DP BARCODE: SUBMISSION CODE:

P.C. CODE: 041405 TOX. CHEM. NO.: 434A

TEST MATERIAL: Sutan Technical (98.2% a.i.).

CITATION: Minor, J.L. et al (1986) Two Generation Reproduction Study in Rats with Sutan. Stauffer Chemical Co. Study No. T-11940, June 18, 1986. MRID No. 00160548 and 00155519.

SPONSOR: Stauffer Chemical Co.

EXECUTIVE SUMMARY: In a 2-generation reproduction study (MRID No. 00160548 and 00155519), Sutan technical (98.2% a.i.) was administered to Sprague-Dawley CD rats (25/sex/dose) in the diet at concentrations of 0, 200, 1000 or 4000 ppm (equivalent to a nominal intake of 0, 10, 50, or 200 mg/kg/day, respectively).

At 4000 ppm, body weights of the parental animals of the Po generation were significantly lower (10-11% for males and 9-14% for females) compared to the controls. Also, body weights of the parental animals of the P1 generation were significantly lower (9-18% for males and 14-19% for females) compared to the controls. At this dose, food consumption of the parental animals of the Po and P1 generations were significantly lower (8-17% for males and 6-21% for females) compared to the controls at most of the reported time intervals. In addition, at this dose, there were decreased hematocrit values in Po males and females, decreased hemoglobin values in Po and P1 females, increased relative liver weights of Po males (13%), Po females (12%) and P1 females. Microscopically, there was an increased incidence of hepatocyte vacuolation in the P1

males.

At 1000 ppm, body weights of dams during gestation (P1, first mating) and during lactation (P1, all matings) were significantly lower (5-8%) compared to the controls. At this dose, there were decreased food consumption of P1 males and increased relative liver weights of Po females (5%).

The NOAEL for parental toxicity was 200 ppm (10 mg/kg/day); the LOAEL was 1000 ppm (50 mg/kg/day) based on decreased food consumption, decreased body weights and increased liver weights (females only).

At 4000 ppm, there was decreased litter size in the F1a, F2a, and F2b generations, decreased absolute kidney weights of F1b males (24%) and F1b females (21%), decreased absolute brain weights of F1b males (10%) and F1b females (8%), decreased kidney weights of F2c males (24%), increased relative liver weights of F2c males and females, increased incidence of dilated kidney (renal pelvis) and retinal folds in the F1b generation.

At 1000 ppm, there were decreased pup weights (8-11%) in the F2a generation on days 14 and 21 and decreased absolute brain (8%) and kidney (15%) weights of the F1b male weanlings.

The NOAEL for reproductive toxicity was 200 ppm (10 mg/kg/day); the LOAEL was 1000 ppm (50 mg/kg/day) based on decreased pup weights and decreased absolute brain and kidney weights.

This study is classified Acceptable/Guideline and satisfies the guideline data requirement for a multi-generation reproduction study (83-4) in rats.

ABSOLUTE AND RELATIVE ORGAN WEIGHTS (grams)(a)

Dose mg/kg/day (ppm)	F1b Male Weanlings (n=5)			P1 Males (n=5)		
	Body wt ±SD	Absolute brain wt ± SD	Relative brain wt (% body wt)	Body wt ± SD	Absolute brain wt ± SD	Relative brain wt (% body wt)
0	82.02 ±3.1	1.657±0.05	2.02	649.3±71.2	2.27±0.09	0.354
10 (200)	***70.16 *±7.0 (86)***	1.554 ±0.11 (93)	***2.22* (110)***	657.0±47.2 (101)	2.27±0.09 (100)	0.347 (98)
50 (1000)	***72.36 *±2.2 (88)***	***1.528*±0.07 (92)***	2.11 (104)	630.8±79.9 (97)	2.23 ±0.12 (98)	0.358 (101)
200 (4000)	***66.16 *±5.7 (81)***	***1.495*±0.06 (90)***	***2.27* (112)***	***588.8*±46.2 (91)***	***2.19*±0.09 (96)***	0.373 (105)
Dose mg/kg/day (ppm)	F1b Female Weanlings (n=5)			P1 Females (n=5)		
	Body wt ± SD	Absolute brain wt ± SD	Relative brain wt (% body wt)	Body wt ± SD	Absolute brain wt± SD	Relative brain wt (% body wt)
0	71.275±3.0	1.516±0.08	2.122	354.0±95.2	2.09±0.09	0.602
10 (200)	75.380±5.2 (10)	1.528±0.04 (101)	2.035 (96)	350.7±32.5 (99)	2.09±0.06 (100)	0.602 (100)
50 (1000)	69.680±7.6 (98)	1.501±0.06 (99)	2.173 (102)	340.2±40.7 (96)	2.06±0.004 (99)	0.605 (100)
200 (4000)	***57.880*±6.6 (81)***	***1.400*±0.09 (92)***	2.434 (115)	***269.8*±20.7 (76)***	***1.98*±0.10 (95)***	***0.685* (114)***

a: Numbers in parentheses are percent of control.
*: Significantly different from control, $p<0.05$.
Source: Tables 40-43, 49A, 49B,57A, and 57B of the Study Report

Supplement to Document # 006875-DER for MRID No. 40389101: A Twelve Month Oral Toxicity Study of Sutan Technical in Dogs. This supplement provides an Executive Summary to upgrade the original DER.

EPA Reviewer: Paul Chin, Ph.D.
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DATA EVALUATION RECORD

STUDY TYPE: 83-1(b) Chronic Feeding Study in Dogs
DP BARCODE: SUBMISSION CODE:
P.C. CODE: 041405 TOX. CHEM. NO.: 434A
TEST MATERIAL: Sutan Technical (concentration stated to be 100% a.i.)
CITATION: Daly, T. W. (1987) A Twelve Month Oral Toxicity Study of Sutan Technical in Dogs. Bio/dynamics Inc., East Millstone, NJ. Study # T-12651. September 14, 1987. MRID No. 40389101. Unpublished.
SPONSOR: Stauffer Chemical Co.

EXECUTIVE SUMMARY:

In a chronic toxicity study (MRID No. 40389101), gelatin capsules containing 0, 5, 25, or 100 mg/kg/day of Sutan technical (100% a.i.) was administered to Beagle dogs (5/sex/dose) for 12 months. Body weight gain (not statistically significant) was reduced in males (17-50%) at 25 mg/kg/day and males (26-50%) and females (20-30%) at 100 mg/kg/day. Both sexes of dogs at 100 mg/kg/day had increased platelet count, increased alkaline phosphatase activity, and increased relative and absolute liver weights. Relative and absolute thyroid/parathyroid weights were increased in high dose males only. There was a statistical increase in relative liver weight in male dogs at 25 mg/kg/day. Additionally hepatocellular vacuolation/vesiculation was observed in 2/5 males (0/5 in controls) in the 100 mg/kg/day group. **The NOAEL for systemic toxicity in males was 5 mg/kg/day. The LOAEL for systemic toxicity was 25 mg/kg/day based on decreased body weight gain and increased relative liver weight in male dogs. The NOAEL for systemic toxicity in females was 25 mg/kg/day; the LOAEL was 100 mg/kg/day based on decreased body weight gain, changes in clinical pathology parameters and increased absolute and relative liver and thyroid/parathyroid weights. This study is classified acceptable/guideline and satisfies the guideline data requirement for a chronic toxicity study (83-1) in dogs.**